REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 1-19, 22 and 25, the only claims pending in this application.

Claim 1 has been amended to recite that the plasma-like solution does not include a conventional biological buffer. Support for these amendments can be found in the specification, e.g., at page 8, paragraph 25. Claim 1 has also been amended to recite that first the level of $C0_2$ is reduced in an amount sufficient to reduce the risk of acidosis/academia, and then the plasma-like solution is administered thereafter. Support for this amendment can be found in the specification, e.g., at page 3, paragraph 12 bridging page 4. Claim 14 and 18 have been amended to remove reference to a conventional biological buffer. Claims 19 and 22 have been amended to recite that the means for reducing the level of $C0_2$ is a pharmacological means that does not include sodium bicarbonate. Support for these amendments can be found in the originally filed claims and in the specification. Claim 22 has also been amended to correct a typographical error wherein "system" has been replaced by "kit" in the preamble. Claims 20-21 and 23-24 have been canceled without prejudice.

As no new matter has been added by the above amendments, the Applicants respectfully request the entry thereof.

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The Examiner has rejected Claims 14 and 18 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. The Examiner asserts that Claims 14 and 18 indicate that they contain a "biological buffer" which renders the claims indefinite as it is uncertain what buffers are and are not included within the scope of the term. The Examiner states that "biological buffer" is not defined by the specification. The term "biological buffer" has been deleted from Claims 14 and 18. In regards to Claims 1, 19 and 22 which have been amended to recite a "conventional biological buffer", the Applicant respectfully submits that the definition of conventional biological buffers is explicitly taught in the specification. For example, the specification at page 8, paragraph 25 teaches:

> The solution of the present invention does not include a conventional biological buffer. By "conventional buffer" is meant a compound that in solution, in vitro, maintains pH at a particular range. By "conventional biological buffer" is meant a compound which in a cell-free system maintains pH in the biological range of 7-8. Examples of conventional biological buffers include N-2-Hydroxyethylpiperazine-N'-2-hydroxypropanesulfonic acid (HEPES), 3-(N-Morpholino) propanesulfonic acid (MOPS), 2-([2-Hydroxy-1,1-bis(hydroxymethyl)ethyl]amino)ethanesulfonic acid (TES), 3-[N-tris(Hydroxy-methyl) ethylamino]-2-hydroxyethyl]-1-piperazinepropanesulfonic acid (EPPS), Tris[hydroxymethyl]-aminomethane (THAM), and Tris[hydroxymethyl]methyl aminomethane (TRIS). Conventional biological buffers have a pK in the physiological range and function most efficiently in this range. Therefore, these buffers function independently of normal biological processes and are most potent in cell-free systems. (emphasis added)

Accordingly, the Applicants respectfully submit that Claims 1, 19 and 22, when read in light of the specification by one skilled in the art, particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. As such, the Applicants respectfully request that this rejection be withdrawn.

REJECTION UNDER 35 U.S.C. §102(b) OR §103(a)

The Examiner has rejected Claims 1-25 under 35 U.S.C. §102(b) as being anticipated by or, in the alternative, under §103(a) as obvious over, Taylor (U.S. Patent No. 5,514,536). The Applicants respectfully submit that the above cited reference does not anticipate Claims 1-25 as amended, nor are Claims 1-25 as amended obvious over the cited reference.

Independent Claim 1 and the claims that depend therefrom have been amended to recite a method of administering a synthetic plasma-like solution that does not include a conventional biological buffer to a subject in need thereof that includes two steps: (a) first reducing the level of CO_2 in a subject in an amount sufficient to reduce the risk of acidosis/acidemia, and (b) then administering a plasma-like solution to the subject.

First and foremost, the Applicant respectfully submits that Taylor does not teach or even suggest the subject claims for at least the reason that Taylor does not teach or suggest a plasma-like solution that does not include a conventional biological buffer. Rather, the invention of Taylor specifically includes a conventional biological buffer (see for example col. 12, lines 12-13). In fact, Taylor specifically

employs a conventional biological buffer (HEPES) specifically described in Applicant's application as a conventional biological buffer not included in the subject invention (see for example page 8, paragraph 25). Accordingly, in addition to the reasons described below, Taylor does not anticipate nor render obvious Claims 1-25 as Taylor teaches the use of a conventional biological buffer and the claims specifically recite that a conventional biological buffer is not included.

While the Applicant believes that the above described-amendment regarding a plasma-like solution that does not include a conventional biological buffer adequately distinguishes the subject claims over Taylor, the Applicant will now also address the Examiner's assertions regarding oxygenators. The Examiner asserts that Taylor inherently teaches that the level of CO_2 in a subject is reduced in an amount sufficient to reduce the risk of acidosis/academia. The Examiner contends that such is inherent in the teachings of Taylor because Taylor teaches that a subject is connected to an oxygenator. The Examiner concludes that since an oxygenator inherently reduces the levels of CO_2, "the burden is on the Applicant to show the prior art method or product cannot produce the same result, i.e., reduction of the risk of acidosis/academia."

In regards to the oxygenator employed by Taylor which the Examiner asserts inherently reduces the level of CO_2 in an amount sufficient to reduce the risk of acidosis/academia because it removes CO_2 from the subject, the Applicant submits that nowhere in Taylor is it taught that the oxygenator reduces the level of CO_2 in an amount sufficient to reduce the risk of acidosis/academia. An inherent characteristic or component is one that necessarily occurs or is present in a component. The Applicant submits that, contrary to the assertion of the Examiner, it is not inherent that the use of an oxygenator reduces the level of CO_2 in a subject. In general, oxygenators add oxygen to, and remove CO_2 from, blood that is pumped through the oxygenator. Accordingly, a variety of factors contribute to the function and performance of an oxygenator. These factors affect the efficiency and/or effectiveness of the oxygenation process. Such factors include, but are not necessarily limited to, the flow rate of the blood through the oxygenator, the gas(es) employed (e.g., the proportion of gases employed), the surface area of the membrane employed in the oxygenator, the dimensions of the membrane employed, the gas transfer efficiencies of the oxygenator, the level of the blood gases in the blood prior to entering the oxygenator, etc. In other words, while oxygenators remove CO_2 from the blood, not all oxygenators remove CO_2 at the same efficiencies and/or effectiveness. In fact, in some instances, a build-up of $C0_2$ in

a subject may occur even with the use of an oxygenator. That is, acidosis/academia may still occur even in instances where an oxygenator is employed to oxygenate the blood of a subject. For example, acidosis/academia may occur even with the use of an oxygenator where the flow of the blood through the oxygenator is too slow and/or the pressure through the oxygenator is too low and/or membrane is too thick and/or does not have sufficient surface area, resulting in an accumulation in the blood of CO_2 and thus resulting in acidosis/academia. Accordingly, even though an oxygenator may be employed in a given procedure, it is in no way inherent that the use of the oxygenator reduces the level of CO_2 in a subject in an amount sufficient to reduce the risk of acidosis/academia.

As further evidence of the fact that it is not inherent that the oxygenator employed in Taylor reduces the level of CO_2 in an amount sufficient to reduce the risk of acidosis/academia, Taylor specifically teaches that HCO_3^- and $H_2PO_4^-$ may be included in the purge solution of Taylor to attempt to combat acidosis (Column 12, lines 16-52), and thus acidosis is not managed by the oxygenator. Accordingly, at best Taylor teaches a method wherein acidosis may be managed by the purge solution itself. Taylor does not, however, teach that the oxygenator disclosed in Taylor reduces the level of CO_2 in a subject in an amount sufficient to reduce the risk of acidosis/academia, as shown by the teaching of the use of HCO_3^- and $H_2PO_4^-$ to manage acidosis. In other words, if the oxygenator of Taylor did indeed reduce the risk of acidosis/academia, there would be no need to describe the management of acidosis/acidemia by the modified purge solution of Taylor.

Accordingly, the Applicant submits that the above description of oxygenators fulfills the requirements suggested by the Examiner in this Office Action. Applicant has explained with particularity the factors that effect the function and performance of an oxygenator and specifically explained that that the use of an oxygenator does not inherently provide a reduction in the level of carbon dioxide in a subject in an amount sufficient to reduce the risk of acidosis/academia as a variety of factors effect the performance of an oxygenator. The Applicants respectfully submit that the above description answers the Examiner's concerns regarding Claims 1-25.

However, if the Examiner believes that the above description of oxygenators does not answer the Examiner's concerns regarding the use of oxygenators and their relation to the subject claims and the Examiner maintains this rejection, the Applicant respectfully requests that the Examiner support the

Examiner's assertion that the use of an oxygenator always results in a reduction in the level of carbon dioxide in a subject in an amount sufficient to reduce the risk of acidosis/academia. In such an instance, the Applicant respectfully requests that the Examiner provide a reference of record or an affidavit signed by the Examiner that supports the Examiner's contention that the use of oxygenators always results in a reduction in the level of carbon dioxide in a subject in an amount sufficient to reduce the risk of acidosis/academia.

Claim 19 has been amended to recite a system that includes two distinct components: (a) a synthetic plasma-like solution that does not comprise a conventional biological buffer, and (b) a pharmacological means that does not include sodium bicarbonate for reducing the CO_2 level of a subject in an amount sufficient to reduce the risk of acidosis/acidemia. As Taylor specifically teaches the use of solutions (purge and maintenance solutions) that include conventional biological buffers, Taylor fails to teach or suggest the system of Claim 19 that recites a plasma-like solution that does not include a conventional biological buffer. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

Claim 22 has been amended to recite a kit that includes two distinct components: (a) a synthetic plasma-like solution that does not comprise a conventional biological buffer, and (b) a pharmacological means that does not include sodium bicarbonate for reducing the CO_2 level of a subject in an amount sufficient to reduce the risk of acidosis/academia. As Taylor specifically teaches the use of solutions (purge and maintenance solutions) that include conventional biological buffers, Taylor fails to teach or suggest the kit of Claim 22 that recites a plasma-like solution that does not include a conventional biological buffer. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

The Examiner has rejected Claims 1-25 under 35 U.S.C. §102(b) as being anticipated by or, in the alternative, under §103(a) as obvious over, Segall et al. (U.S. Patent No. 5,702,880) or Segall et al. (U.S. Patent No. 5,571,801). The Applicants respectfully submit that neither of the above cited references anticipates Claims 1-25 as amended, nor are claims 1-25 as amended obvious over either of the cited references.

As described above, independent Claim 1 and the claims that depend therefrom have been amended to recite a method of administering a synthetic plasma-like solution that does not include a conventional biological buffer to a subject in need thereof that includes two steps: (a) first reducing the level of CO_2 in a subject in an amount sufficient to reduce the risk of acidosis/acidemia, and (b) then administering a plasma-like solution to the subject.

As the Examiner notes, Segall et al. teach a method of administering a blood substitute. However, neither the '801 patent nor the '880 patent teach the two step method of Claim 1, namely a method of (a) first reducing the level of CO_2 in a subject in an amount sufficient to reduce the risk of acidosis/acidemia, and (b) then administering a plasma-like solution to the subject.

While the cited references disclose placing a subject on an oxygenator, it is not taught in these references that either results in a reduction of the level of CO_2 in the subject in an amount sufficient to reduce the risk of acidosis/academia. Analogous to that described above in regards to the Taylor reference, nowhere in either of these references is it taught that the use of the oxygenator reduces the level of CO_2 in an amount sufficient to reduce the risk of acidosis/academia. As explained above, it is not inherent that the use of an oxygenator results in a reduction of the level of CO_2 in the subject in an amount sufficient to reduce the risk of acidosis/academia.

Furthermore, in regard to the '801 patent, as further support that the oxygenator does not reduce the level of CO_2 in an amount sufficient to reduce the risk of acidosis/academia, the patent describes that sodium bicarbonate may be administered as needed to manage acidosis (see Column 19, lines 66-67). In other words, the management of acidosis, as described in the '801 patent, occurs after the procedure has been completed, in fact it occurs after the incisions are closed (Column 19, lines 65-66) such that acidosis management occurs post-operatively by the use of sodium bicarbonate – not the oxygenator. The Examiner contends that the sodium bicarbonate is only "used if needed". However, the Applicant concurs with the Examiner in that if acidosis is in need of management, the '801 patent teaches that sodium bicarbonate may be administered post-operatively. In other words, it is not taught in the '801 patent that the oxygenator employed in this patent reduces $C0_2$ in an amount sufficient to reduce the risk of acidosis/academia, but rather it is specifically taught that acidosis may be managed post-operatively by sodium bicarbonate, if needed. It is important to note that the post-operative use of sodium

bicarbonate still does not anticipate the subject claims nor render the subject claims obvious as the claimed two step method including first reducing the level of CO_2 in the subject in an amount sufficient to reduce the risk of acidosis/academia and then administering a plasma-like solution is not taught or suggested in the '801 patent and in fact the '801 patent only teaches a method of first administering a solution and then, if needed, employing sodium bicarbonate post-operatively to manage acidosis. In regards to the '880 patent, this patent fails to even discuss acidosis/acidemia. As explained above, an oxygenator does not inherently result in a reduction of the level of CO_2 in the subject in an amount sufficient to reduce the risk of acidosis/academia.

As such, both the '801 patent and the '880 patent fail to teach or even suggest each and every claimed limitation and thus neither cited reference anticipates nor renders obvious Claim 1 and the claims that depend therefrom. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

In regards to independent Claim 19 and the claims that depend therefrom, Claim 19 has been amended to recite a system that includes two distinct items: (a) a synthetic plasma-like solution that does not include a conventional biological buffer, and (b) a pharmacological means that does not include sodium bicarbonate for reducing the CO_2 level of a subject in an amount sufficient to reduce the risk of acidosis/acidemia. For reasons analogous to those described above, i.e., both the '801 patent and the '880 patent fail to teach a system that includes a pharmacological means that is not sodium bicarbonate for reducing the CO_2 level of a subject in an amount sufficient to reduce the risk of acidosis/acidemia, neither reference anticipates nor renders obvious Claim 19 and the claims that depend therefrom. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

In regards to Claim 22, as described above, independent Claim 22 has been amended to recite that the kit includes a pharmacological means that is not sodium bicarbonate for reducing the CO_2 level of a subject in an amount sufficient to reduce the risk of acidosis/acidemia. Accordingly, for reasons analogous to those described above, i.e., because neither cited reference teaches a kit that includes a pharmacological means that is not sodium bicarbonate for reducing the CO_2 level of a subject in an amount sufficient to reduce the risk of acidosis/academia, neither the '801 patent nor the '880 patent

anticipates nor renders obvious Claim 22 and the claims that depend therefrom. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In view of the remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815, reference no. BIOT-008.

Respectfully submitted,
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Date: 3/3/03

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